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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,739	11/18/2003	Murugan R. Pandian	054769-6702	6774

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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
09/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,739	PANDIAN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The Request for Continued Examination filed July 30, 2007 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54-56, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological material is (1) known and readily available to the public; (2) reproducible from the written description, e.g. sequenced; or (3) deposited.

Claims 54-56, 63 and 64 are directed to a method that uses monoclonal antibodies designated B152 and/or B207. It is apparent that the hybridoma secreting these monoclonal antibodies are required to practice the claimed invention. As required elements, the hybridoma producing the monoclonal antibodies must be known and be readily available to the public, or obtainable by a reproducible method set forth in the specification, or otherwise be readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the hybridoma producing the monoclonal antibodies. From the instant specification, it appears that the hybridomas producing the monoclonal antibodies designated as B152 (p. 8, lines 10-24) and B207 (p. 10, lines 8-24) are

deposited at a recognized depository. The monoclonal antibodies do not appear to be readily available to the public, and it is unclear if the hybridoma cell lines producing the monoclonal antibodies of the recited binding specificity can be reproducibly isolated without undue experimentation. Since obtaining such monoclonal antibodies having the recited binding specificity is uncertain and non-predictable, undue experimentation would have been required to practice the invention as claimed. Without a publicly available deposit of hybridoma cell lines producing the above-identified monoclonal antibodies, one of skill in the art could not be assured of the ability to practice the invention as claimed. A deposit of the hybridoma producing the monoclonal antibodies designated as B152 and B207 would satisfy the requirements of 35 U.S.C. § 112, first paragraph. Further, as indicated by a search in the ATCC of the Accession Numbers hb-12467 and PTA 1626 provided in the current application. The ATCC indicates that the accession numbers were not found in the catalog (see ATCC, product description attached).

If deposits have already been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application, and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is

necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each state.

The claim(s) should be amended with the proper information regarding the deposit number and provide evidence to support the insertion for the depository number. As a means of satisfying the necessary criteria of the deposit rules and to show that the deposited hybridoma cell lines producing the recited monoclonal antibodies are the same as the ones deposited, Applicants may submit a copy of the contract or notice of acceptance of the cell line(s) by the depository.

Applicants' attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 C.F.R § 1.801-1.809 for further information concerning deposit practice.

It is noted that the claims also include clones 820 and 827. However, as indicated by applicant in the specification on page 8, the monoclonal antibody clone 820 is publicly available from Biodesign International, Saco, Maine (Catalog Number E45550M). Also, clone 820 is available and can be purchased through AMS biotechnology, product code E45550M (see attachment) and through biocompare, The Buyer's Guide for Life Scientists (see attachment). Page 9 of the specification also indicates that the monoclonal antibody clone 827 is publicly available from Biodesign International, Saco, Maine (Catalog Number E45575M). Also, clone 827 is available through Gentaur, catalog number E45575M (see page 12), and through biocompare, The Buyer's Guide for Life Scientists (see attachment). Thus, clones 820 and 827 are known and readily available.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 51-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 is vague and indefinite because of the use of acronyms: i.e. ITA and hCG. Although the terms may have art-recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The terms should be defined in their first instance. See also deficiency found in claims 63 and 64.

Claim 51, line 11 the recitation "the elevated signal" there is insufficient antecedent support for this limitation.

Claim 51 steps (i-ii) is vague and indefinite in the method because it is unclear how the method would work without a step of separation or washing to remove unbound ITA or hCG, or unbound detection antibody. Without a separation or wash step there would always be detection antibody present and thus there would always be a positive reaction. Therefore, it appears that the method would always give positive results. See for example pages 21, 22 and 25 of the specification which require a separation step. Please clarify.

Claim 53 is vague and indefinite because it contradicts claim 51. Claim 51 requires a confirmation step that the subject is not pregnant. However, claim 53 requires that the trophoblastic disease is a hydatidiform mole which is known to be a pathologic condition of pregnancy (see definition hydatidiform mole provided in the

office action mailed 08/23/06). Therefore, it is unclear how one can detect a pathologic condition of pregnancy when the subject is confirmed to be not pregnant.

Claim 63, line 12 the recitation "the elevated signal" there is insufficient antecedent support for this limitation. See also deficiency found in claim 64.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 51-59, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (Clinical Chemistry 47:2, 308-315, Feb. 2001) in view of O'Connor et al (US 6,500,627) in light of Birken et al (Immunochemical measurement of Early Pregnancy Isofoms of hCG: Potential Applications to Fertility Research, Prenatal Diagnosis, and Cancer, 32 (2001) 635-643) in view of Hochstrasser et al (US 2003/0157580) and Chin et al (US 2002/0142305) and further in view of Bellet et al (US 2002/0192646).

Cole et al disclose human chorionic gonadotropin immunoassays in the diagnosis of trophoblastic diseases. Cole et al disclose that patients with trophoblastic disease produce ordinary and irregular forms of human chorionic gonadotropin (p. 308). Cole et al disclose that trophoblastic disease include complete and partial hydatidiform mole, postmolar tumor, gestational choriocarcinoma, testicular choriocarcinoma, and placental site trophoblastic disease (p. 309). Cole et al discloses that patients can be diagnosed with choriocarcinoma solely from a persistent positive hCG result, in the absence of a pregnancy (p. 314). Cole et al is generic with respect to the reagents used in the immunoassay.

Cole et al differ from the instant invention in failing to specifically state the use of antibodies to the hyperglycosylated human chorionic gonadotropin (ITA) and human chorionic gonadotropin (hCG) and also fails to teach labels in the immunoassay in one assay.

O'Connor et al (US 6,500,627) disclose methods of detecting trophoblastic disease. O'Connor et al disclose that the trophoblastic disease can include choriocarcinoma or hydatidiform mole. O'Connor et al disclose contacting a sample from a subject with an antibody which specifically binds to a molecular isoform of hCG. O'Connor et al disclose contacting the sample with a second antibody which specifically binds to intact non-nicked hCG (hCG) (col 4 and col 25-26). O'Connor et al disclose B152 antibodies specific for the isoform of hCG (ITA) (col 10, lines 40-44). Birken et al (Archives of Medical Research, 2001, 635-643) disclose that B152 is hyperglycosylated form (abstract). Therefore, O'Connor et al teaches detecting hyperglycosylated hCG (ITA). O'Connor et al disclose that the amount of B152 isoform (hyperglycosylated hCG) and hCG are increased in trophoblast disease (col 25-26). O'Connor et al also disclose that hCG is elevated in pregnancy. O'Connor et al discloses that the sample can be a blood, serum or urine sample. O'Connor et al disclose using two capture antibodies B152 (same as used by applicant) and B108 or B109) (col 7, line 38- col 8). O'Connor et al disclose that detection can be performed by using a labeled antibody (detection antibody) and also teaches that the detection antibody can be B207 (same as used by applicant). O'Connor et al disclose that the label can be a radioactive isotope such as I^{125}.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate antibodies and labels as taught by O'Connor et al into the method of diagnosing as taught by Cole et al because Cole et al specifically teaches that immunoassays are used for diagnosing trophoblastic disease and

O'Connor et al teaches specific antibodies and labels used in immunoassays for diagnosing trophoblastic disease. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antibodies and labels as taught by O'Connor et al into the method of Cole et al.

Cole et al and O'Connor et al fail to teach confirming the subject is not pregnant. Cole et al and O'Connor et al also differs from the instant invention in failing to teach comparing the signal generated in the sample to a signal generated in a sample obtained from a normal, non-pregnant subject.

Since Cole et al specifically teaches that non-pregnant subjects can be diagnosed with trophoblastic disease and also since the combination of Cole et al and O'Connor et al disclose that hyperglycosylated hCG (ITA) and hCG are elevated in both trophoblastic disease and pregnancy one of ordinary skill in the art would consider that pregnancy would have to be excluded before determining trophoblastic disease and thus would confirm that the patient was not pregnant before determining trophoblastic disease. Further, Hochstrasser et al (abstract & page 1, paragraph 0012) teaches that in order to perform diagnostic assays on markers which are known to be involved in more than one condition, one must be able to distinguish between the two conditions and thus perform an assay to exclude one of the conditions. Therefore, it would have been obvious to one of ordinary skill in the art to confirm that the subject is not pregnant before detecting a trophoblastic disease.

Chin et al teaches that it is known in the art of diagnostics to establish baseline levels and controls using individuals of the same population as that of the

subject to be tested (para. 0166) and further teaches using these levels to provide a means for comparison to the levels of that of the tested subject (paragraphs 0166 & 0167). Chin et al teaches that this provides for the determination of positive results and also provides for optimizing diagnostic assays.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate baselines and controls of normal healthy subjects as taught by Chin et al into the modified method of Cole et al because Cole et al is silent with respect to the diagnostic steps and Chin et al teaches that it is known in the art to establish baseline levels and controls using individuals of the same population as that of the subject to be tested and also teaches that this provides for the determination of positive results and also provides for optimizing diagnostic assays. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating baseline levels and controls as taught by Chin et al into the modified method of Cole et al.

Cole et al. O'Connor and Chin et al fail to teach the normal individual is a non-pregnant individual.

Bellet et al disclose that the levels of hCG or of the free hCGa subunit is greater in patients having a tumor of trophoblastic origin than that of non-pregnant healthy individuals (para. 0002).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate non-pregnant healthy individuals as taught by Bellet et al into the modified method of Cole et al because the modified method of Cole would

be excluding pregnant patients and Chin et al teaches that it is known in the art to establish baseline levels and controls using individuals of the same population as that of the subject to be tested. Thus, one of ordinary skill in the art would want to incorporate a non-pregnant healthy patient as a control into the modified method of Cole and one of ordinary skill in the art would have a reasonable expectation of success incorporating non-pregnant healthy patients into the modified method of Cole et al.

With respect to the recitations "clone 827" and "clone 820" as recited in the current claims. There is no conventional method for naming antibodies therefore, Examiner interprets the B108 and B109 capture antibodies disclosed in O'Connor to be the same as the 827 and 820 clones recited by Applicant. Further, the Patent and Trademark Office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference, in the first place between the antibodies of O'Conner et al and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430(CCPA 1977).

Regarding the interpretive "wherein" clause recited in claims 51, 63 and 64 ("wherein the elevated signal in the sample relative to the sample from the normal, non-pregnant subject indicates trophoblastic disease in the subject", the clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results to those steps. Therefore, the "wherein" clause is not considered to further limit the method defined by the claim and has not been given

weight in construing the claims. See Texas Instruments, Inc. v. International Trade Comm., 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A whereby clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim."). See also Minton v. National Assoc. of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) ("A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.").

8. Claims 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al in view of O'Connor et al (US 6,500,627), Hochstrasser et al (US 2003/0157580), Chin et al (US 2002/0142305), Bellet et al (US 2002/0192646) and further in view of Campbell et al (US 4,946,958).

See above for teachings of Cole et al., O'Connor et al., Hochstrasser et al., Chin et al., and Bellet et al.

Cole et al., O'Connor et al., Hochstrasser et al., Chin et al and Bellet et al differ from the instant invention in failing to teach the assay is a chmiluminescent assay.

Campbell et al disclose a chemiluminescent label comprising an acridinium ester which is conveniently linked to a monoclonal antibody or other protein and is used in immunoassay for the quantitation of an antigen of interest (abstract). Campbell et al disclose that the use of this chemiluminescent label in assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude (col 7, lines 27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chemiluminescent label as taught by Campbell et al for the label of O'Connor et al because Campbell et al shows that the use of this chemiluminescent label in two-site assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude.

With respect to claim 62. The combination of references disclose the claimed invention except for the assay is automated. It would have been obvious to one having ordinary skill in the art at the time the invention was made to automate the modified method of Cole, since it has been held that broadly providing a mechanical or automatic means to replace manual activity which has accomplished the same result involves only routine skill in the art. *In re Venner,* 120 USPQ 192.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
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Art Unit 1641
August 21, 2007

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